Remarks

The Rejection of Claims 8-10 Under 35 U.S.C. § 101

Claims 8-10 have been rejected under 35 U.S.C. § 101 as not having an apparent or disclosed specific, substantial, and credible utility. Applicant respectfully traverses the rejection.

Independent claim 8 is directed to a purified polypeptide comprising the amino acid sequence shown in SEQ ID NO:2. Dependent claim 9 is directed to a purified polypeptide consisting of the recited amino acid sequence. Claim 10 is directed to a fusion protein comprising a polypeptide having the amino acid sequence shown in SEQ ID NO:2.

The utility requirement for a claimed invention is met if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention and if the utility is specific, substantial, and credible. Manual of Patent Examining Procedure (M.P.E.P.) § 2107(II), 8th ed. The Office Action asserts that the claimed polypeptides do not meet this standard because there is no evidence of record that the claimed polypeptides have a "biological significance" or an association with a disease or disorder. Paper 11, page 4, lines 3-8.

The specification discloses utilities for the claimed polypeptides that are specific, substantial, and credible. First, a claimed invention has a specific and substantial utility if the application discloses a particular biological activity and explains how that activity can be used in a particular therapeutic application. M.P.E.P. § 2107.02(II)(A). The specification discloses several particular biological activities of the claimed human lipoxin A_4 receptor-like polypeptides. The specification discloses that human lipoxin A_4 receptor-like polypeptides "bind lipoxin A_4, or a lipoxin A_4 analog and . . . mediate a biological effect, such as cyclic AMP formation, mobilization of intracellular calcium or phosphinositide metabolism." Page 9, lines

9-11. The specification also discloses that lipoxin A_4, by signaling through a lipoxin A_4 receptor polypeptide, has the particular biological activities of affecting vascular smooth muscle and systemic immune responses. The specification teaches that

> [l]ipoxin A_4 has been shown to contract pulmonary smooth muscle (guinea pig lung), but not guinea pig ileum or trachea, and to relax (dilate) vascular smooth muscle at concentrations of less than 1 μM. Topical administration of lipoxin A_4 to the hamster cheek pouch induces a pronounced arteriolar dilation, but does not change venular diameters. Lipoxin A_4 has also been shown to induce neutrophils to generate superoxide radicals, release elastase, and promote chemotaxis by leukocytes.

Page 3, line 27 to page 4, line 5, citations omitted. The specification teaches that, through binding lipoxin A_4 receptor-like polypeptide to lipoxin A_4, the activity of the claimed polypeptides can affect vascular smooth muscle responses.

The specification also discloses how the biological activities of the claimed polypeptides can be used in particular therapeutic applications, specifically to treat conditions requiring control of vascular smooth muscle or unwanted systemic immune responses. The specification teaches that "[r]egulators of lipoxin A4 receptor-like polypeptide can be used to control hemostasis, vascular reactivity, especially vasoconstriction, and anaphylactic and allergic reactions." Page 8, lines 15-17.

The specification discloses a particular biological activity for the claimed human lipoxin A_4 receptor-like polypeptides and explains how that activity can be used in a particular therapeutic application. The specification therefore discloses a specific and substantial utility for the claimed polypeptides.

Second, the asserted utility of a claimed invention is credible unless (A) the logic underlying the assertion is seriously flawed or (B) the facts upon which the assertion is based are

inconsistent with the logic underlying the assertion. M.P.E.P. § 2107.02(III)(B). The application discloses characteristics of the claimed human lipoxin A_4 receptor-like polypeptides that support its teachings that these polypeptides are useful for the control of hemostasis, vascular reactivity (especially vasoconstriction), and anaphylactic and allergic reactions. The specification discloses that the polypeptide of SEQ ID NO:2 comprises seven transmembrane domains, which is characteristic of other lipoxin A_4 receptors. As shown in Exhibit A, the amino acid sequence of SEQ ID NO:2 ("Query") aligns with the amino acid sequence of Gorilla low affinity N-formyl peptide receptor ("Subject") with 27% identity and 47% homology. Lipoxin A_4 and N-formyl peptide receptors are known to be very closely related (see Exhibit B, at the receptors designated FML1_HUMAN:FPRL1, lines 2-3; FML1_MOUSE:FPRLI, lines 5-6; and O88536, line 25), and N-formyl peptide receptors bind lipoxin (Vaughn *et al., J. Immunol.* (2002) *169*:3363-3369, lines 19-20 of the Abstract; Exhibit C). Thus it cannot be asserted that the logic underlying the assertion of the claimed polypeptides' utility is flawed or that the facts underlying the assertion of the claimed polypeptides' utility are inconsistent with the logic underlying the asserted utility.

The Office Action provides Skolnick (*TIBTECH* (2000) *18*:34-39) and Yan (*Science* (2000) *290*:523-527) to support that its position that one of skill in the art would doubt the credibility of the asserted utility for the lipoxin A_4 receptor-like polypeptides. Skolnick is cited as teaching that "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function." Paper 11, page 4, lines 9-11, quoting Skolnick at page 36, box 2. Skolnick teaches five protein structures that do not necessarily predict function: the immunoglobulin-like fold, the flavodoxin-like fold, the knottins, the triose-phosphate isomerase barrels, and the ferredoxin-like fold. See page 36, Figure 1 in Box 2. The claimed polypeptides do not contain any of these structures.

Thus, Skolnick does not provide any specific teaching that negates the credibility of the asserted utility of the claimed polypeptides.

Yan is cited as teaching "that even [a] two-amino acid substitution in a molecular structure of a protein can lead to a total loss [in the ability] of a protein to bind a specific receptor." Paper 11, page 4, lines 12-14. Yan teaches two isoforms of ectodysplasin, EDA-A1 and EDA-A2, that differ by an insertion of two amino acids. Page 523, lines 3-5 of the Abstract. The ectodysplasin isoforms bind to two different receptors. "EDA-A1 binds only the receptor EDAR, whereas EDA-A2 binds only the related, but distinct, X-linked ectodysplasin-A2 receptor (XEDAR)." Page 523, lines 6-8. EDAR and XEDAR, however, are both members of the TNFR superfamily. See Yan at page 523, column 1, lines 7-8 and page 524, column 1, lines 48-49. Thus even though the ectodysplasin ligand isoforms bind to two different receptors, they are both still TNFR superfamily ligands. Thus it is also credible that the claimed polypeptides are also members of the lipoxin A_4 receptor-like polypeptide superfamily.

Applicant respectfully requests withdrawal of this rejection.

The Rejection of Claims 8-10 Under 35 U.S.C. § 112

Claims 8-10 have been rejected under 35 U.S.C. § 112 as not enabled. Applicant respectfully traverses the rejection.

The Office Action asserts that "since the claimed invention is not supported by either a clear asserted utility or a well established utility . . . one skilled in the art would not know how to use the claimed invention." Paper 11, page 6, lines 1-4. In response to the rejection under 35 U.S.C. § 101, Applicant has demonstrated that the claimed polypeptides have utility, mooting the asserted basis of the rejection.

Applicant respectfully requests withdrawal of this rejection.

The Rejection of Claims 8 and 9 Under 35 U.S.C. § 102(a)

Claims 8 and 9 have been rejected under 35 U.S.C. § 102(a) as anticipated by Elshourbagy *et al.*, WO 00/26339 ("Elshourbagy"). Applicant respectfully traverses the rejection.

United States Code Title 35, section 102 states that:

> A person shall be entitled to a patent unless—
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.

Elshourbagy is cited as teaching an amino acid sequence that is 100% identical to SEQ ID NO:2. Paper 11, page 6, lines 14-15. Elshourbagy, however, is not prior art to the present application. Elshourbagy was published on May 11, 2000. The priority date of the present application is March 14, 2000. The Patent Office asserts that the present application is not entitled to its priority date of March 14, 2000 because the claimed polypeptides lack utility and therefore are not enabled. However, as demonstrated above, the claimed invention has utility. The application is entitled to its priority date of March 14, 2000. Thus, Elshourbagy does not anticipate claims 8 and 9.

Applicant respectfully requests withdrawal of this rejection.

The Rejection of Claim 10 Under 35 U.S.C. § 103(a)

Claim 10 stands rejected under 35 U.S.C. § 103(a) as obvious over Elshourbagy in view of Hopp *et al.*, U.S. Patent 5,011,912 ("Hopp"). Applicant respectfully traverses the rejection.

A *prima facie* case of obviousness has not been made because, as demonstrated above, Elshourbagy is not prior art to the present application.

Applicant respectfully requests withdrawal of this rejection.

Respectfully submitted,

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By:_____
Lisa M. Hemmendinger
Registration No. 42,653

BANNER & WITCOFF, LTD.
1001 G. Street, N.W.
Eleventh Floor
Washington, D.C. 20001
(202) 508-9100